STATEMENT
OF
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ON BEHALF OF
THE AMERICAN LIVER FOUNDATION (ALF)

AND

THE GREATER WASHINGTON DC CHAPTER

PROVIDED TO
THE NONPRESCRIPTION DRUG ADVISORY COMMITTEE
OF THE US FOOD AND DRUG ADMINISTRATION

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Good afternoon and thank you for the opportunity to provide testimony here today. My name is Dr. Caroline Riely and I'm a professor of medicine and pediatrics at the University of Tennessee College of Medicine.

I am providing testimony today on behalf of the American Liver Foundation -- a leading national voluntary health agency dedicated to the prevention, treatment and cure of hepatitis and other liver diseases through research, education, and advocacy. We are here today because we are concerned about the issue of adverse reactions in the liver to over-the-counter medications.

As a hepatologist caring for patients with both acute and chronic liver disease, I suggest both acetaminophen and non-steroidal anti-inflammatory drugs such as ibuprofen to my patients, depending on the setting. For example, acetaminophen is the antipyretic and analgesic of choice for patients with chronic non-alcohol related liver disease, despite it's well known association with hepatotoxicity, particularly in alcoholics. Ibuprofen is not a hepatotoxin, but can be toxic to the kidneys in patients with chronic liver disease.

Acetaminophen, normally a very safe drug, is a hepatotoxin when taken in the right dose in the right setting. The therapeutic window for this agent is narrow – the usual adult dose is 1 gram (2 pills) PO q 4 hours, but a single dose of 20 grams (40 pills) can cause lethal hepatotoxicity. And, persons who chronically use alcohol can have toxicity at a dose as low as 4 GM (8 pills) per day.

Acetaminophen is a constituent of many combination medications, both over the counter and prescribed. So a patient may take 2 forms of acetaminophen without being aware of that fact – for example, a patient may use Tylenol PM and Percocet, and may inadvertently exceed the safe dose.

This is particularly a problem in the pediatric population. In this group the formulations change with age, but the parent may not be aware that the preparation advised for an infant – to take one dropper full, is quite different than the preparation for children – and cannot be dosed in the same fashion [more here to be inserted by Dr. Sokol].

We are concerned that marketing practices make it very difficult to find the lower dose, 325 mg, in drug stores or discount store shelves. The consumer thinks that an extra strength acetaminophen product is the only strength available. Given the narrow therapeutic window, this failure to market the lower dose may contribute to increased adverse events.

At the American Liver Foundation, we would like to encourage an active approach to this problem, and would like to participate in any way we can. There needs to be greater awareness on the part of all, the consumer (or their parents), the pharmacist, and the physician providing primary care for the consumer. We would advocate an innovative educational effort to help minimize this problem. For example, the package warnings in use now are too small, difficult to read, and felt to be unimportant. An educational effort

aimed at the site of purchase would be useful. There could be signs or brochures, in Spanish as well as English, available at the display shelf, or at the check out counter. Pharmacists distributing acetaminophen-containing prescription drugs, such as Percocet, should label the bottle to indicate that the medication contains acetaminophen, and that toxic doses may be attained if the patient is an alcohol user, or taking OTC acetaminophen. Public service announcements on TV would be helpful. And, the manufacturers should promote the use of the 325 mg tablets, or at least give them equal shelf space, with some informative guidelines as to which dose is appropriate for whom.

Likewise, physician education is important. Physicians need to know ALL of the medications, both OTC and prescribed, that their patients are taking. They need to be aware of the narrow therapeutic window for acetaminophen, and its interaction with alcohol. And pediatricians and family practitioners should go over with parents the appropriate dosing for the various pediatric formulations

We realize that discussion of over the counter medications in patients with chronic diseases is tomorrow's topic. The ALF would like to take this opportunity to remind the panel that NSAIDS, but not acetaminophen, are potentially toxic in patients with chronic liver disease, leading to renal failure at modest doses.

Acetaminophen is a good drug, proven so over decades. Efforts at education of the consumer and the professional will result in an even better safety record for this agent.

Thank you very much for allowing me this opportunity to share the American Liver Foundation's views with you today.

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